Express Mail No.:EL018081509US

Claims

1. A method for inducing T cell receptor gene rearrangement, comprising:

contacting a T cell with a CD40-binding agent that binds CD40 in an amount sufficient to induce T cell receptor gene rearrangement in the T cell.

2. The method of claim 1, wherein the T cell is present in a lymphocyte population enriched for T cells.

3. The method of claim 2, wherein the lymphocyte population enriched for T cells is further enriched for T cells by selectively eliminating B cells.

4. The method of claim 2, wherein the lymphocyte population enriched for T cells contains at least 50% T cells.

5. The method of claim 2, wherein the lymphocyte population enriched for T cells contains at least 75% T cells.

6. The method of claim 2, wherein the lymphocyte population enriched for T cells contains at least 90% T cells.

7. The method of claim 2, wherein the lymphocyte population enriched for T cells contains at least 95% T cells.

8. The method of claim 1, wherein contacting of the T cell with a CD40-binding agent that binds CD40 occurs *in vitro*.

9. The method of claim 1, wherein contacting of the T cell with a CD40-binding agent that binds CD40 occurs *ex vivo*.

10. The method of claim 1, wherein the T cell is derived from an *in vitro* culture of hematopoietic cells.

11. The method of claim 1, wherein the CD40-binding agent comprises at least two agents:

i) a first agent that binds a first CD40 receptor, and

ii) a second crosslinking agent that crosslinks the first agent to at least a second receptor selected from the group consisting of a second CD40 receptor and a T cell receptor.

12. The method of claim 11, wherein the first agent that binds a first CD40 receptor is selected from the group consisting of a CD40 ligand and an anti-CD40 antibody.

13. The method of claim 11, wherein the second crosslinking agent that crosslinks the first agent to the second receptor is selected from the group consisting of a CD40 ligand, an anti-CD40 antibody and an antigen.

14. The method of claim 12, wherein the CD40 ligand is the polypeptide of SEQ ID NO:2 or a fragment thereof.

15. The method of claim 13, wherein the CD40 ligand is the polypeptide of SEQ ID NO:2 or a fragment thereof.

16. The method of claim 1, wherein the T cell is of a $CD69^{+}TCR^{+}$ phenotype.

17. The method of claim 1, wherein the T cell is of a phenotype selected from the group consisting of $CD4^{lo}CD8^{lo}CD69^{+}TCR^{+}$, $CD4^{lo}CD8^{hi}CD69^{+}TCR^{+}$, and $CD4^{hi}CD8^{lo}CD69^{+}TCR^{+}$.

18. The method of claims 1-17, further comprising administering a co-stimulatory agent, wherein the co-stimulatory agent is selected from the group consisting of a co-stimulatory molecule and a cytokine.

19. The method of claim 18, wherein the co-stimulatory molecule is selected from the group consisting of TSA-1, CD2, CD5, CD24, CD28, CD49a, CD80, CD81 and CD86.

20. The method of claim 18, wherein the cytokine is selected from the group consisting of IL-2 and IL-4.

21. A method for promoting T cell maturation, comprising:

contacting an immature T cell with a CD40-binding agent that binds CD40 in an amount sufficient to promote maturation of the immature T cell.

22. The method of claim 21, wherein the T cell is present in a lymphocyte population enriched for T cells.

23. The method of claim 22, wherein the lymphocyte population enriched for T cells is further enriched for T cells by selectively eliminating B cells.

24. The method of claim 22, wherein the lymphocyte population enriched for T cells contains at least 50% T cells.

25. The method of claim 22, wherein the lymphocyte population enriched for T cells contains at least 75% T cells.

26. The method of claim 22, wherein the lymphocyte population enriched for T cells contains at least 90% T cells.

27. The method of claim 22, wherein the lymphocyte population enriched for T cells contains at least 95% T cells.

28. The method of claim 21, wherein contacting of the T cell with a CD40-binding agent that binds CD40 occurs *in vitro*.

29. The method of claim 21, wherein contacting of the T cell with a CD40-binding agent that binds CD40 occurs *ex vivo*.

30. The method of claim 21, wherein the T cell is derived from an *in vitro* culture of hematopoietic cells.

31. The method of claim 21, wherein the CD40-binding agent comprises at least two agents:

i) a first agent that binds a first CD40 receptor, and

ii) a second crosslinking agent that crosslinks the first agent to at least a second receptor selected from the group consisting of a second CD40 receptor and a T cell receptor.

32. The method of claim 31, wherein the first agent that binds a first CD40 receptor is selected from the group consisting of a CD40 ligand and an anti-CD40 antibody.

33. The method of claim 31, wherein the second crosslinking agent that crosslinks the first agent to the second receptor is selected from the group consisting of a CD40 ligand, an anti-CD40 antibody and an antigen.

34. The method of claim 32, wherein the CD40 ligand is the polypeptide of SEQ ID NO:2 or a fragment thereof.

35. The method of claim 33, wherein the CD40 ligand is the polypeptide of SEQ ID NO:2 or a fragment thereof.

36. The method of claim 21, wherein the T cell is of a $CD69^{-}TCR^{lo}$ phenotype.

37. The method of claim 21, wherein the T cell is of a phenotype selected from the group consisting of $CD4^{+}CD8^{+}TCR^{lo}$, and $CD117^{+}TCR^{lo}$.

38. The method of claims 21-37, further comprising administering a co-stimulatory agent, wherein the co-stimulatory agent is selected from the group consisting of a co-stimulatory molecule and a cytokine.

39. The method of claim 38, wherein the co-stimulatory molecule is selected from the group consisting of TSA-1, CD2, CD5, CD24, CD28, CD49a, CD80, CD81 and CD86.

40. The method of claim 38, wherein the cytokine is selected from the group consisting of IL-2 and IL-4.

41. A method for inhibiting T cell receptor gene rearrangement, comprising:

contacting a T cell expressing CD40 with an agent that inhibits CD40-induced T cell receptor rearrangement.

42. The method of claim 41, wherein contacting of the T cell expressing CD40 with an agent that inhibits CD40-induced T cell receptor rearrangement occurs *in vitro*.

43. The method of claim 41, wherein contacting of the T cell expressing CD40 with an agent that inhibits CD40-induced T cell receptor rearrangement occurs *ex vivo*.

44. The method of claim 41, wherein the T cell is derived from an *in vitro* culture of hematopoietic cells.

46. The method of claim 41, wherein the agent that inhibits CD40-induced T cell receptor rearrangement is selected from the group consisting of an anti-CD40 ligand antibody, a soluble CD40 ligand antagonist, and a NF-κB inhibitor.

47. A method for inducing T cell reactivity toward an antigen, comprising:

introducing an amount of T cells and an amount of antigen presenting cells into a culture vessel, and

co-culturing the T cells and the antigen presenting cells in the presence of:

(i) a CD40-binding agent that binds CD40 in an amount sufficient to induce T cell receptor gene rearrangement in the T cells, and

(ii) at least one antigen,

under conditions sufficient to induce the formation of T cells having specificity for the at least one antigen.

48. The method of claim 47, wherein the T cell is present in a lymphocyte population enriched for T cells.

49. The method of claim 48, wherein the lymphocyte population enriched for T cells is further enriched for T cells by selectively eliminating B cells.

50. The method of claim 48, wherein the lymphocyte population enriched for T cells contains at least 50% T cells.

51. The method of claim 48, wherein the lymphocyte population enriched for T cells contains at least 75% T cells.

52. The method of claim 48, wherein the lymphocyte population enriched for T cells contains at least 90% T cells.

53. The method of claim 48, wherein the lymphocyte population enriched for T cells contains at least 95% T cells.

54. The method of claim 47, wherein contacting of the T cell with a CD40-binding agent that binds CD40 occurs *in vitro*.

55. The method of claim 47, wherein contacting of the T cell with a CD40-binding agent that binds CD40 occurs *ex vivo*.

56. The method of claim 47, wherein the T cell is derived from an *in vitro* culture of hematopoietic cells.

57. The method of claim 47, wherein the CD40-binding agent comprises at least two agents:

i) a first agent that binds a first CD40 receptor, and

ii) a second crosslinking agent that crosslinks the first agent to at least a second receptor selected from the group consisting of a second CD40 receptor and a T cell receptor.

58. The method of claim 57, wherein the first agent that binds a first CD40 receptor is selected from the group consisting of a CD40 ligand and an anti-CD40 antibody.

59. The method of claim 57, wherein the second crosslinking agent that crosslinks the first agent to the second receptor is selected from the group consisting of a CD40 ligand, an anti-CD40 antibody and an antigen.

60. The method of claim 58, wherein the CD40 ligand is the polypeptide of SEQ ID NO:2 or a fragment thereof.

61. The method of claim 59, wherein the CD40 ligand is the polypeptide of SEQ ID NO:2 or a fragment thereof.

62. The method of claim 47, wherein the T cell is of a $CD69^{+}TCR^{+}$ phenotype.

63. The method of claim 47, wherein the T cell is of a phenotype selected from the group consisting of $CD4^{lo}CD8^{lo}CD69^{+}TCR^{+}$, $CD4^{lo}CD8^{hi}CD69^{+}TCR^{+}$, and $CD4^{hi}CD8^{lo}CD69^{+}TCR^{+}$.

64. The method of claims 47-63, further comprising administering a co-stimulatory agent, wherein the co-stimulatory agent is selected from the group consisting of a co-stimulatory molecule and a cytokine.

65. The method of claim 64, wherein the co-stimulatory molecule is selected from the group consisting of TSA-1, CD2, CD5, CD24, CD28, CD49a, CD80, CD81 and CD86.

66. The method of claim 64, wherein the cytokine is selected from the group consisting of IL-2 and IL-4.

67. A method for inhibiting environmental stress-induced cell-death of a T cell, comprising:

contacting a T cell expressing CD40, under environmental stress otherwise sufficient to induce cell-death, with a CD40-binding agent that binds CD40 and induces T cell receptor gene rearrangement in an amount sufficient to inhibit death of the cell expressing CD40 which otherwise would result from the environmental stress.

68. The method of claim 67, wherein the T cell is present in a lymphocyte population enriched for T cells.

69. The method of claim 68, wherein the lymphocyte population enriched for T cells is further enriched for T cells by selectively eliminating B cells.

70. The method of claim 68, wherein the lymphocyte population enriched for T cells contains at least 50% T cells.

71. The method of claim 68, wherein the lymphocyte population enriched for T cells contains at least 75% T cells.

72. The method of claim 68, wherein the lymphocyte population enriched for T cells contains at least 90% T cells.

73. The method of claim 68, wherein the lymphocyte population enriched for T cells contains at least 95% T cells.

74. The method of claim 67, wherein contacting of the T cell with a CD40-binding agent that binds CD40 occurs *in vitro*.

75. The method of claim 67, wherein contacting of the T cell with a CD40-binding agent that binds CD40 occurs *ex vivo*.

76. The method of claim 67, wherein the T cell is derived from an *in vitro* culture of hematopoietic cells.

77. The method of claim 67, wherein the CD40-binding agent comprises at least two agents:

i) a first agent that binds a first CD40 receptor, and

ii) second crosslinking agent that crosslinks the first agent to at least a second receptor selected from the group consisting of a second CD40 receptor and a T cell receptor.

78. The method of claim 77, wherein the first agent that binds a first CD40 receptor is selected from the group consisting of a CD40 ligand and an anti-CD40 antibody.

79. The method of claim 77, wherein the second crosslinking agent that crosslinks the first agent to the second receptor is selected from the group consisting of a CD40 ligand, an anti-CD40 antibody and an antigen.

80. The method of claim 78, wherein the CD40 ligand is the polypeptide of SEQ ID NO:2 or a fragment thereof.

81. The method of claim 79, wherein the CD40 ligand is the polypeptide of SEQ ID NO:2 or a fragment thereof.

82. The method of claim 67, wherein the T cell is of a phenotype selected from the group consisting of $CD69^{+}TCR^{+}$, $CD4^{lo}CD8^{lo}CD69^{+}TCR^{+}$, $CD4^{lo}CD8^{hi}CD69^{+}TCR^{+}$, and $CD4^{hi}CD8^{lo}CD69^{+}TCR^{+}$.

83. The method of claim 67, wherein the T cell is of a phenotype selected from the group consisting of $CD69^{-}TCR^{lo}$, $CD4^{+}CD8^{+}TCR^{lo}$, and $CD117^{+}TCR^{lo}$.

84. The method of claim 67, wherein the environmental stress is selected from the group consisting of chemical stress, physical stress, oxidative stress, and γ-irradiation.

85. A method for enhancing environmental stress-induced T cell-death, comprising:

contacting a T cell expressing CD40 with a CD40-binding agent that binds CD40 in an amount sufficient to induce T cell receptor gene rearrangement,

subjecting the CD40-binding agent bound T cell to an environmental stress sufficient to induce cell-death.

86. The method of claim 85, wherein the T cell is present in a lymphocyte population enriched for T cells.

87. The method of claim 86, wherein the lymphocyte population enriched for T cells is further enriched for T cells by selectively eliminating B cells.

88. The method of claim 86, wherein the lymphocyte population enriched for T cells contains at least 50% T cells.

89. The method of claim 86, wherein the lymphocyte population enriched for T cells contains at least 75% T cells.

90. The method of claim 86, wherein the lymphocyte population enriched for T cells contains at least 90% T cells.

91. The method of claim 86, wherein the lymphocyte population enriched for T cells contains at least 95% T cells.

92. The method of claim 85, wherein contacting of the T cell with a CD40-binding agent that binds CD40 occurs *in vitro*.

93. The method of claim 85, wherein contacting of the T cell with a CD40-binding agent that binds CD40 occurs *ex vivo*.

94. The method of claim 85, wherein the T cell is derived from an *in vitro* culture of hematopoietic cells.

95. The method of claim 85, wherein the CD40-binding agent comprises at least two agents:

i) a first agent that binds a first CD40 receptor, and

ii) a second crosslinking agent that crosslinks the first agent to at least a second receptor selected from the group consisting of a second CD40 receptor and a T cell receptor.

96. The method of claim 95, wherein the first agent that binds a first CD40 receptor is selected from the group consisting of a CD40 ligand and an anti-CD40 antibody.

97. The method of claim 95, wherein the second crosslinking agent that crosslinks the first agent to the second receptor is selected from the group consisting of a CD40 ligand, an anti-CD40 antibody and an antigen.

98. The method of claim 96, wherein the CD40 ligand is the polypeptide of SEQ ID NO:2 or a fragment thereof.

99. The method of claim 97, wherein the CD40 ligand is the polypeptide of SEQ ID NO:2 or a fragment thereof.

100. The method of claim 85, wherein the T cell is of a phenotype selected from the group consisting of $CD69^{+}TCR^{+}$, $CD4^{lo}CD8^{lo}CD69^{+}TCR^{+}$, $CD4^{lo}CD8^{hi}CD69^{+}TCR^{+}$, and $CD4^{hi}CD8^{lo}CD69^{+}TCR^{+}$.

101. The method of claim 85, wherein the T cell is of a phenotype selected from the group consisting of $CD69^{-}TCR^{lo}$, $CD4^{+}CD8^{+}TCR^{lo}$, and $CD117^{+}TCR^{lo}$.

102. The method of claim 85, wherein the environmental stress is selected from the group consisting of chemical stress, physical stress, oxidative stress, and γ-irradiation.

103. The method of claim 85, wherein the T cell is selected from the group consisting of a cancerous T cell and a self-reactive T cell, and the environmental stress is a chemotherapeutic agent.